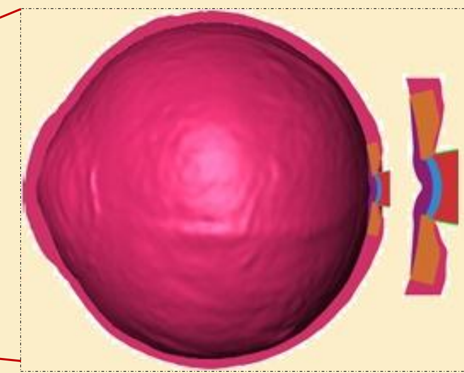
MODELS OF THE EYE: RELEVANCE TO MICROGRAVITY INDUCED VISUAL IMPAIRMENT AND INTRACRANIAL PRESSURE



62nd International Astronautical Congress

Human Space Endeavours Virtual Forum: The Next 50 Years

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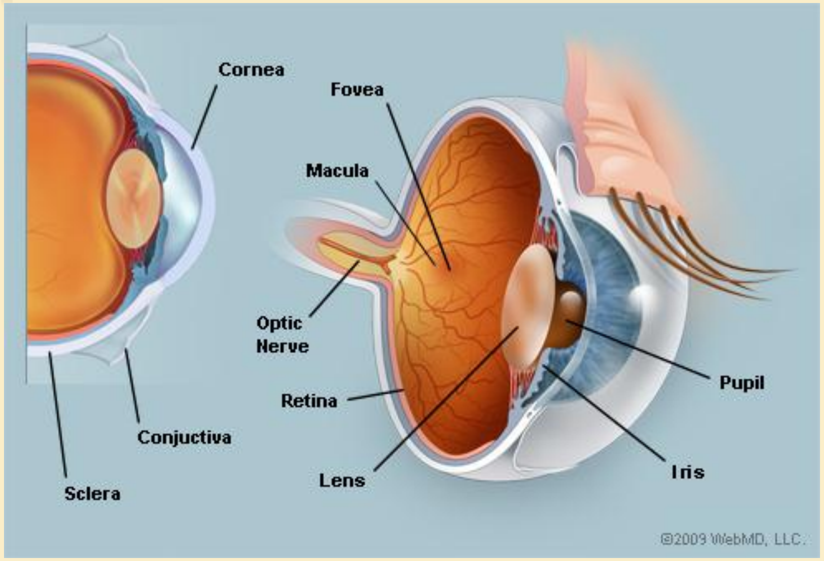
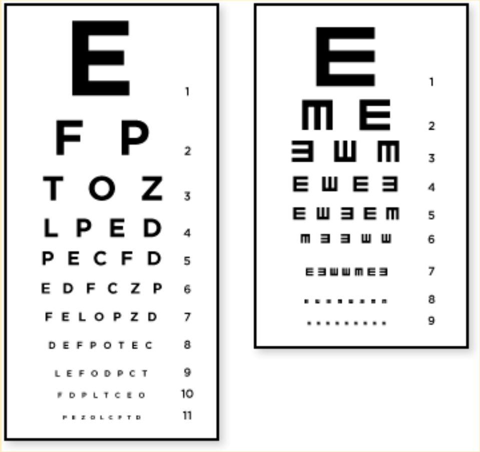
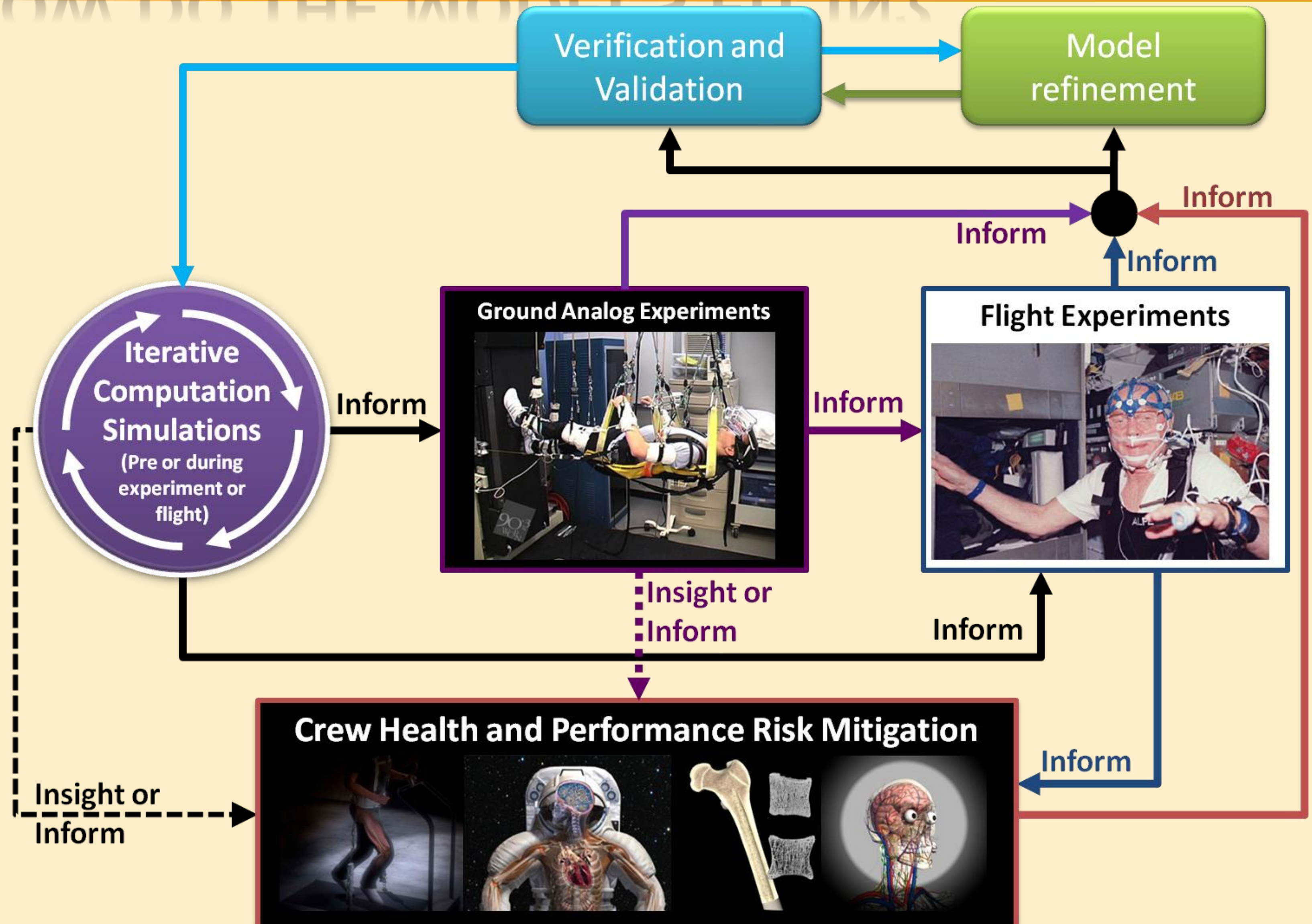
IMPORTANCE OF MODELS IN STUDYING THE EYE

- Allows for a deeper understanding of the eye
  - How Intraocular Pressure (IOP) and mechanical property changes affect stress/strain in the eye
- Allow for possible prediction of outcomes in astronauts based on eye health





HOW DO THE MODELS FIT IN?



GAPS TO BE ADDRESSED

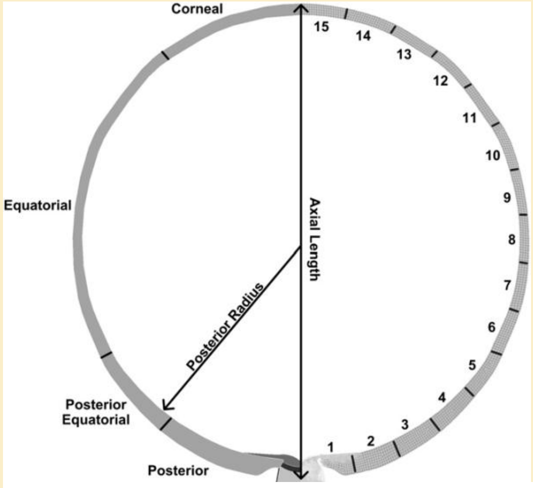
- **Gap (VIIP2)** Does exposure to microgravity cause changes in visual acuity, intraocular pressure and/or intracranial pressure? Are the effects related to mission duration?
- **Gap (VIIP4)** Are changes in visual acuity related to changes in chronic choroidal engorgement, elevated intraocular pressure and/or intracranial pressure?

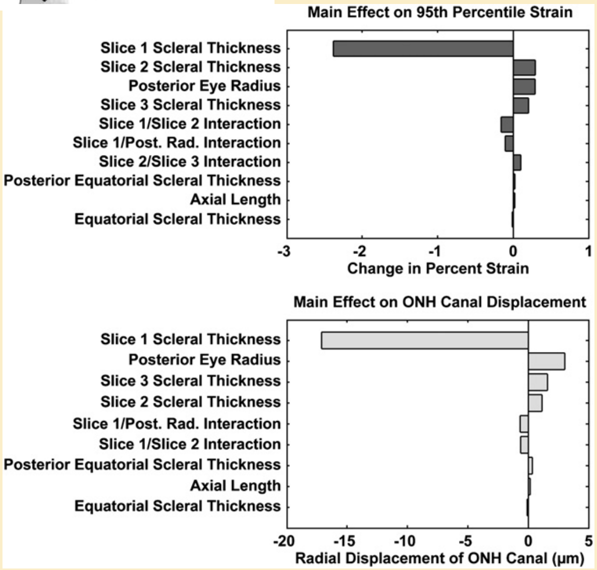
THREE PAPERS

- Finite element modeling of the human sclera: Influence on optic nerve head biomechanics and connections with glaucoma
- The optic nerve head as a biomechanical structure: initial finite element modeling
- Factors Influencing Optic Nerve Head Biomechanics

FINITE ELEMENT MODELING OF THE HUMAN SCLERA

- Individual specific corneoscleral shell parameters paired with idealized ONH
  - P1 – 2.4-4.6
  - P2 – 1.6-3.2
  - P3 – -3.8 - -7.3
- Sensitivity analysis conducted using idealized scleral and ONH





THE OPTIC NERVE HEAD AS A BIOMECHANICAL STRUCTURE: INITIAL FINITE ELEMENT MODELING

- Thirteen digital 3D geometries representing idealized human eyes were studied
- Models were varied in scleral wall thickness, scleral canal shape, and inner radius
- Measured stress at 15 mm Hg IOP

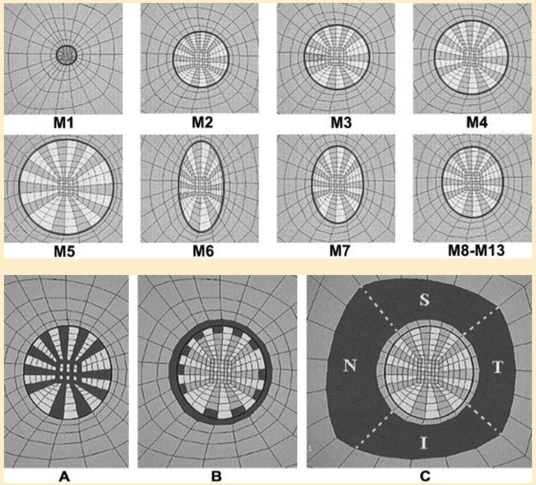


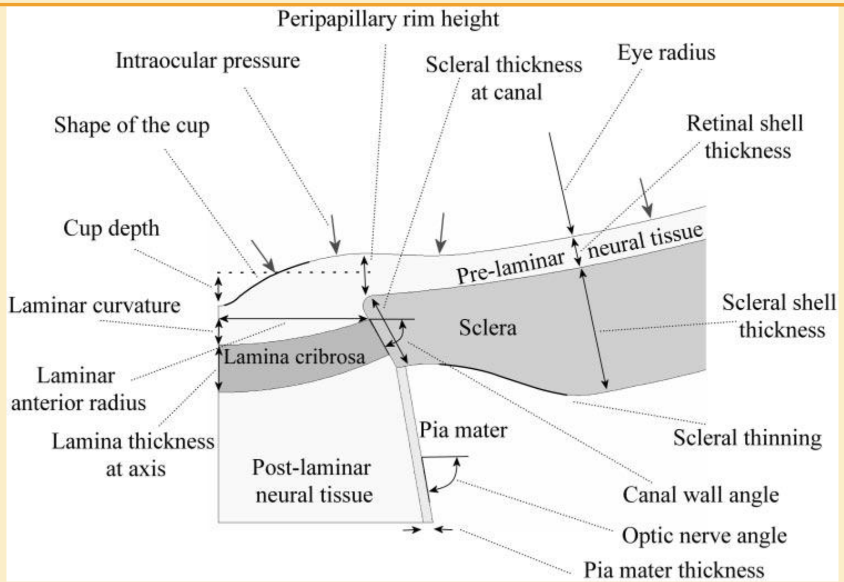
TABLE 3. Summary of the Maximum Stress Levels Expressed as Multiples of IOP

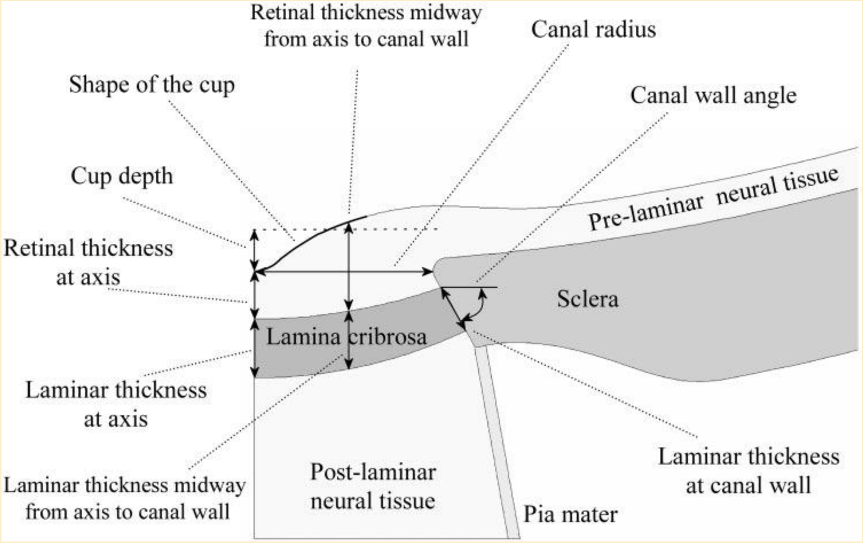
Model	Posterior Sclera	Peripapillary Sclera	Laminar Insertion Zone	Laminar Trabeculae
Circular				
M1 (0.50 × 0.50)	11	11	20	34
M2 (1.50 × 1.50)	11	15	31	54
M3 (1.75 × 1.75)	11	16	34	65
M4 (2.00 × 2.00)	11	17	38	77
M5 (2.56 × 2.56)	11	20	47	107
Elliptical				
M6 (2.50 × 1.25)	11	21	40	72
M7 (2.10 × 1.40)	11	17	35	65
M8 (1.92 × 1.67)	11	16	35	67
Wall thickness				
M9 (0.5)	17	27	63	122
M8 (0.8)	11	16	35	67
M10 (1.0)	9	13	27	50
M11 (1.5)	6	8	16	28
Inner radius				
M8 (12.0)	11	16	35	67
M12 (13.0)	12	17	36	66
M13 (14.0)	13	18	38	66

All dimensions shown in millimeters. Data are the means of the highest 5% of stress magnitude values (from Table 2) expressed as multiples of IOP.

FACTORS INFLUENCING OPTIC NERVE HEAD BIOMECHANICS

- Detailed sensitivity analysis of ONH to various input factors
- Measured outcomes via different output factors

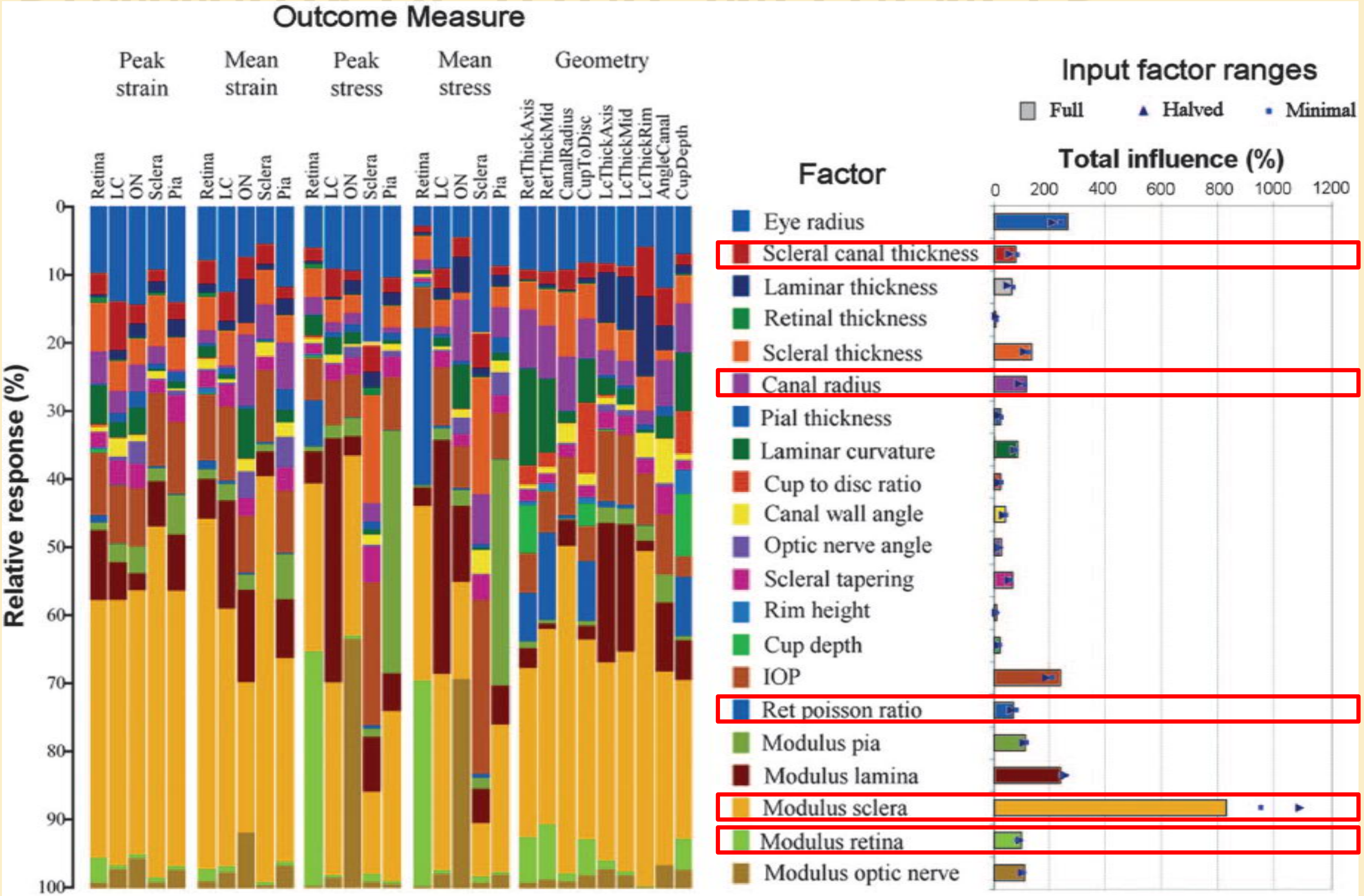




METHOD OF COMPARISON BETWEEN INPUT FACTORS

- Absolute response - the range of outcomes by varying only one input factor of a particular outcome
- Total response - the sum of the absolute responses for one particular outcome
- Relative response - absolute response of one factor divided by the total response
- Total influence – sum of relative responses of single input over all outcomes

SUMMARY OF TOTAL INFLUENCES



OTHER IMPORTANT INFORMATION

TABLE 1. Histomorphometric Measurements of the Lamina Cribrosa

	Control Group	Glaucoma Group	P
n	42	11	
Lamina cribrosa thickness (μm)			
Central region	457.7 ± 163.7	201.5 ± 251.5	<0.001
Median	464.0	75	
Range	92–1008	39–868	
Midperipheral region	463.3 ± 167.6	173.3 ± 191.2	<0.001
Median	441.5	62	
Range	133–1013	30–684	
Midperipheral region	461.3 ± 189.6	188.9 ± 241.3	<0.001
Median	441.0	84	
Range	111–1353	28–850	
Peripheral region	435.3 ± 130.6	161.4 ± 184.2	<0.001
Median	447.0	99	
Range	82–714	38–658	
Peripheral region	464.9 ± 190.6	162.6 ± 194.1	<0.001
Median	457.5	60	
Range	71–1290	33–663	
Ratio of inner to outer lamina cribrosa surface	0.88 ± 0.12	0.99 ± 0.05	0.002
Median	0.87	1.0	
Range	0.57–1.35	0.85–1.0	
Length of the posterior surface of the lamina cribrosa directly exposed to the pia mater and indirectly to the cerebrospinal fluid space (μm)	39.4 ± 99.6	310.2 ± 299.0	<0.001
Median	0	321	
Range	0–334	0–842	
Shortest distance (μm) between inner surface of the lamina cribrosa and cerebrospinal fluid space	847.0 ± 224.8	606.9 ± 382.3	<0.001
Median	810.5	511	
Range	384–1488	307–1710	
Shortest distance (μm) between inner surface of the lamina cribrosa and inner surface of the pia mater	557.9 ± 172.1	335.4 ± 266.6	<0.001
Median	546.0	314	
Range	185–998	99–1079	

Data are expressed as the mean ± SD. *P* is the significance of the differences (Mann-Whitney test) between the two study groups.

Relative Distances b/t structures in the eye - “Anatomic Relationship between Lamina Cribrosa, Intraocular Space, and Cerebrospinal fluid Space” – Jonas et al.

TABLE 1. Summary of Mechanical Properties of ONH Tissues

Tissue/Species	Author(s)	Young's Modulus (MPa)
Sclera		
Tree Shrew	Phillips and McBrien[23]	2.28
Tree Shrew	Siegwart and Norton[24]	0.69–18.3
Bovine	Smolek[25]	3.8–9.0
Human	Woo et al.[26]	5.5
Human	Friberg and Lace[27]	1.8–2.9
Monkey	Downs et al.[28]	2.9–5.5
Porcine	Spörl E, et al. *IOVS* 2003;44:ARVO E-Abstract 3318	0.3
Human	Battaglioli and Kamm[29]	4.76
Human	Kobayashi et al.[30]	5.5
Neural tissue		
Porcine brain	Miller[31]	0.03
Bovine brain	Guillaume et al.[32]	0.046
Monkey brain	Merz et al.[33]	0.010
Bovine retina	Jones et al.[34]	0.020
Cat spinal cord	Chang et al.[35]	0.2–0.6
Rabbit spinal cord	Ozawa et al.[36]	0.035
Lamina cribrosa		
Porcine	Spörl E, et al. *IOVS* 2003;44:ARVO E-Abstract 3318	0.1
Fit to human	Edwards and Good[6]	0.14–0.38
Monkey	Bellezza et al.[37]	0.077–0.405
Pia mater		
Human	Zhivoderov et al.*[38]	1.44–4.65
Human	Our computations based on measurements by Mazuchowski and Thibault[39]	2.5–65
Human	Brands[40]	1.86 (Shear modulus)

The Young's moduli chosen for this study were: sclera, 3 MPa; lamina cribrosa, 0.3 MPa; neural tissue, 0.03 MPa; pia mater, 3 MPa; and central retinal vessels, 0.3 MPa. Results of a parametric study based on these values are shown in Figure 7.

* As cited by Kleiven.[41]

Mechanical Properties of the human eye “Finite Element Modeling of Optic Nerve Head Biomechanics” – Sigal et al.

MORE MATERIALS PROPERTIES

Table 1. Input Factors and Their Baseline Values and Ranges Used in the Sensitivity Analysis (see Figure 1 for Factor Definitions)

Name	Coded Name	Units	Baseline	Low	High	Sources
Input factors defining the geometry of the eye and ONH						
Internal radius of eye shell	EyeRadius	mm	12.0	9.6	14.4	9–13
Scleral thickness at canal	ScThickAtCanal	mm	0.4	0.32	0.48	13–16
Laminar thickness at axis	LCThickAxis	mm	0.3	0.24	0.36	13,16–18
Retinal thickness	RetThickShell	mm	0.2	0.16	0.24	19,20
Scleral shell thickness	ScThickShell	mm	0.8	0.64	0.96	11,14,15
LC anterior surface radius	LCRadius	mm	0.95	0.76	1.14	10,12,13,16,18,21–24
Pia mater thickness	PiaThick	mm	0.06	0.048	0.072	13
Laminar curvature	LCDepth	mm	0.2	0	0.2	*
Cup-to-disc ratio/shape of the cup	Cup2DiscRatio	—	0.25	0.1	0.5	19,21
Canal wall angle to the horizontal	AngleScCanal	deg	60	48	72	*
Optic nerve angle	AngleON	deg	80	64	96	*
Scleral thinning/peripapillary scleral tapering	ScThinFactor	—	0.5	0	1.0	11,15
Peripapillary rim height	RimHeight	mm	0.3	0.24	0.36	19,21,25
Cup depth	CupDepth	mm	0.33	0.26	0.4	19,21
Input factors defining the load on ONH tissues						
Intraocular pressure	IOP	mm Hg	25	20	30	26,27
Input factors defining the biomechanical properties of relevant optic tissues						
Poisson ratio of retina	RetPoisson	—	0.49	0.4	0.49	28–30
Pia mater Young's modulus	PiaModulus	MPa	3	1	9	31–33
Lamina cribrosa Young's modulus	LCModulus	MPa	0.3	0.1	0.9	6,34–36
Sclera Young's modulus	ScModulus	MPa	3	1	9	29,37–44,54
Retina Young's modulus	RetModulus	MPa	0.03	0.01	0.09	45–50
Optic nerve Young's modulus	ONModulus	MPa	0.03	0.01	0.09	Same as for retina

Ranges were estimated from our own measurements (*), or from a combination of our measurements and the sources listed (see the Methods section for details). In many cases, the sources did not directly measure the quantity of interest. In such situations, we computed the quantity of interest from the data that were reported.

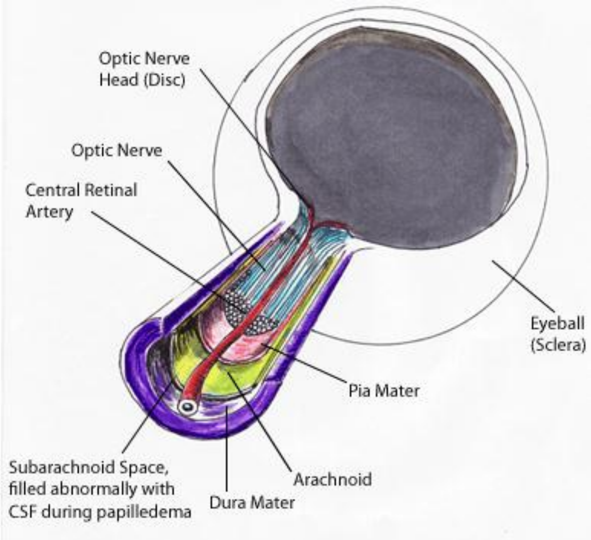
Mechanical Properties of the human eye
"Factors Influencing Optic Nerve Head
Biomechanics– Sigal et al.

ASSUMPTIONS AND CONSIDERATIONS

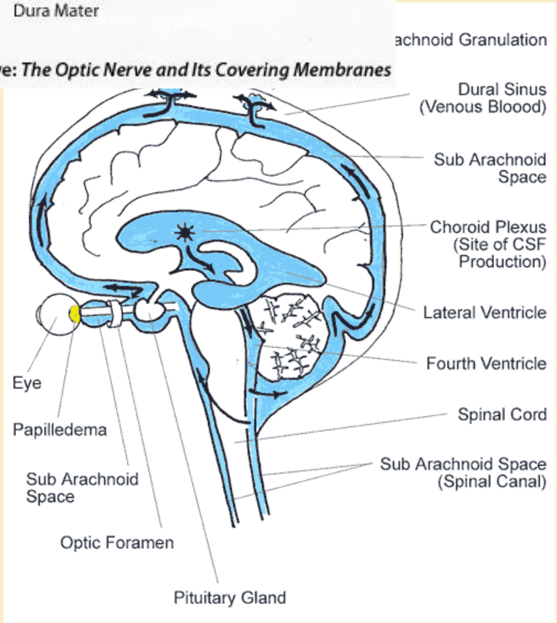
- Several simplifications
  - Geometries
  - Linear materials properties
  - Ignores some important aspects of structure, such as the non-homogeneity nature of the various tissues
- Future work needed
  - Obtain non-linear materials properties
  - Account for non-homogeneity in structures
  - Make shapes of the eye more realistic

CONNECTION WITH THE BRAIN AND ICP

- CSF acts on optic nerve of eye
  - Compress nerve and vasculature
  - Push against lamina cribrosa
- Effects on ON not understood
- Pressure against LC causes deformation and can disrupt trans-laminar pressure
- Possibility of segregation of CSF due to increased ICP



Posterior View of Eye: *The Optic Nerve and Its Covering Membranes*



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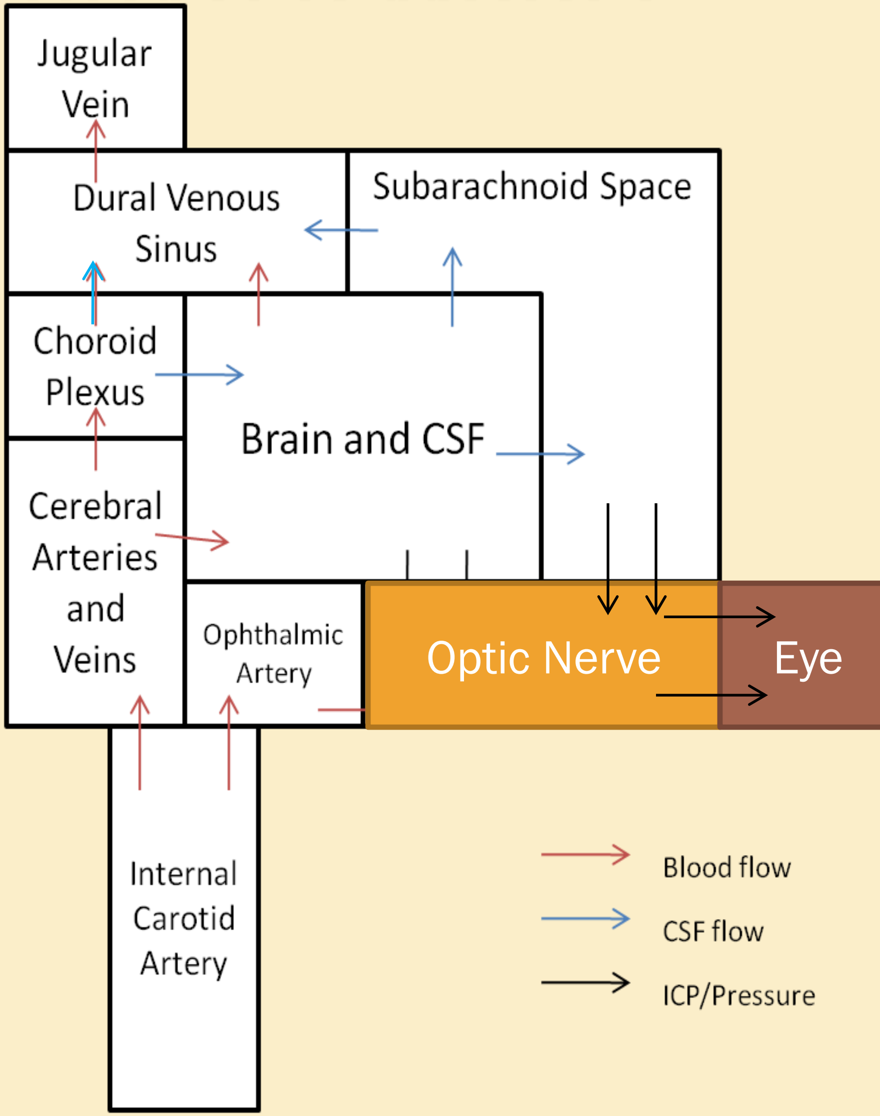
RECOMMENDATIONS

- For design of the model
  - Begin with the current linear materials properties currently in literature → good starting point
  - Use an idealized geometry
  - Integrate eye model with brain/CSF as single model or through inputs/outputs
- Once a simplified model is created
  - Account for realistic structure of the eye → Jonas et al.
  - Find or measure non-linear viscoelastic properties

PRELIMINARY VIIP INTEGRATED MODEL

- Based on 7-compartment model proposed by Sorek et al.
- Accounts for interactions between vascular and cerebral fluid systems



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